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APPLICATION NO.	FILING DATE	FIRST	NAMED INVENTOR	ATTORNEY DOCKET NO.
08/509,359	07/31/95	ST. GEO	RGE-HYSLOP P	CAN-004

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EXAMINER	
ALLEN,M	

ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev. 2/95)

Office Action Summary	Application No. 08/509,359	Applicant(s) St. George-Hyslop
	Examiner Marianne Allen	Group Art Unit 1818

☒ Responsive to communication(s) filed on *May 27, 1997* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *24, 25, and 71-76* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *24, 25, 71, 72, and 74-76* is/are rejected.

☒ Claim(s) *73* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *9, 12, 17*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Claims 1-23 and 26-70 have been cancelled. Claims 73-76 have been newly introduced. Claims 24-25 and 71-76 are pending and under consideration by the examiner.

Applicant is requested to complete the reference to the prior applications inserted as the first sentence of the specification of this application if applicant intends to rely on the filing date of the prior applications under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a).

The disclosure is objected to because of the following informalities: .

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with one or more of the requirements of 37 CFR § 1.821 through 1.825.

The sequences disclosed in Tables 3, 5, and 8 and on pages 48 and 66 do not appear to be referenced by SEQ ID NO. It is not clear whether the sequences are present in the sequence listing.

References to the SEQ ID NOS. in the specification appear to be incomplete and/or incorrect. For example, oligonucleotides disclosed on page 63 are referenced as SEQ ID NO: 138-141; however, these oligonucleotides do not correspond to these SEQ ID NOS. The sequence listing contains 160 sequences; however, only a handful of these are referenced in the specification. (See also new matter rejection below.)

It is noted that any corrections to the sequence listing will require submission of a new CRF. A new sequence listing will need to be submitted to replace the present one in the specification. A statement that the content of the paper and computer readable copies are the same and contain no new matter would also need to be submitted.

Appropriate correction is required.

The amendment filed 29 February 1996 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The amendment filed 29 February 1996 added a sequence listing containing 160 sequences to the specification. This sequence listing replaced original pages 76-164 which disclosed sequences but which were not in the proper format. However, the original pages and the sequence listing submitted do not correspond. For example, SEQ ID NO: 137 on original page 152 is an amino acid sequence of approximately 450 amino acids and in the sequence listing filed 29 February 1996 SEQ ID NO: 137 is a nucleotide sequence of 2285 base pairs. Similarly, SEQ ID NO: 138 on original page 153 is an oligonucleotide primer and in the sequence listing filed 29 February 1996 SEQ ID NO: 138 is a 448 amino acid sequence.

Applicant is requested to review the original specification carefully and determine whether all of the referenced sequences correspond to those disclosed in the sequence listing. If applicant

has merely renumbered the sequences **all** of the specification references should be amended accordingly.

Applicant is required to cancel the new matter in the response to this Office action.

Claims 24-25, 71-72, and 74-76 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for E5-1 proteins having the sequence of SEQ ID NO: 138 (wild type protein) and SEQ ID NO: 138 wherein the Asn at amino acid position 141 has been replaced by Ile and/or wherein the Met at amino acid position 239 has been replaced by Val (naturally occurring mutants), does not reasonably provide enablement for other E5-1 proteins encompassed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not appear to disclose a specific use for the purified E5-1 protein, variants, or muteins thereof. However, it may be inferred from the specification that antibodies to the naturally occurring proteins (wild-type and naturally occurring mutants) may be of use as reagents in diagnostic assays for Alzheimer's disease. This does not provide a disclosure of how to use other variants, muteins, or functionally conserved variants encompassed by the claims. Such proteins could not be used in a diagnostic setting because they do not naturally occur and thus antibodies raised against them would not be predictive of the presence or absence of any medical condition.

In addition, the specification does not disclose the metes and bounds of "functional fragment" or "functionally conserved variant." That is, the biological activity of the E5-1 protein is not disclosed and no assay appears to be disclosed such that one of ordinary skill in the art could determine when the limitations of the claims have been met.

The specification discloses the human E5-1 protein of SEQ ID NO: 138 and naturally occurring mutants of this human E5-1 wherein the Asn at amino acid position 141 has been replaced by Ile and/or wherein the Met at amino acid position 239 has been replaced by Val. No other naturally occurring mutants have been identified. These specific proteins meet the written description and enablement provisions of 35 USC 112, first paragraph. However, the claims are directed to or encompass sequences from other species, mutated sequences, and so forth. None of these sequences meets the written description provision of 35 USC 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the sequences discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed proteins and therefore conception is not

achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself (which would identify the encoded protein) is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, only SEQ ID NO: 138 and the two specifically identified mutations (Asn->Ile at 141 and Met->Val at 239) but not the full breadth of the claim meets the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

With respect to the named positions for mutation, the specification does not disclose that these mutations and/or numbered amino acid positions occur in any other protein. The specification does not disclose how related proteins would correspond with respect to their numbering.

Claims 72 and 74-76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 72, listing amino acid positions for mutation in the absence of reference to a specific sequence is indefinite. The named amino acid positions only have meaning in the context of SEQ ID NO: 138.

Claim 74 recites specific mutations with respect to SEQ ID NO: 138; however, claim 71 (upon which it depends) is not limited to the protein of SEQ ID NO: 138 and so the claim is confusing.

Claim 76 is confusing in its dependency on claim 73. It appears that this claim should depend from claim 74. Claim 74 is limited to a specific SEQ ID NO. As written, claim 76 would not have all of the limitations of claim 73.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 24-25 and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over L'Hernault et al.

L'Hernault et al. discloses the membrane spanning SPE-4 protein, mutants thereof, and DNA sequence from chromosome I of *C. elegans*. The effects of gene expression on spermatogenesis are disclosed. (See abstract and Figures 7 and 9.) The reference does not disclose substantially purifying the protein.

It would have been obvious to take the nucleic acid sequence of the SPE-4 protein as taught by L'Hernault et al., produce the protein recombinantly using well known techniques, and substantially purify it using well known techniques. One would have been motivated to do so in order to further characterize the protein and its role in spermatogenesis.

The specification fails to define the metes and bounds of an E5-1 protein or variant or functionally conserved variant. As such, the SPE-4 protein from *C. elegans* disclosed by L'Hernault et al. is deemed to meet the limitations of the claims. Note that the specification at page 28 concedes its structural similarity.

Applicant is advised that based upon their response to this Office action clarifying the claims and intended metes and bounds of the E5-1 protein and functional variants, double patenting rejections may be made over claims in co-pending applications to ARMP proteins. That is, the ARMP protein appears to be within the definition of a mutein, functional variant, and/or functionally conserved variant. Absent a specific definition for E5-1 protein, this general name for a family of proteins could also be construed to include the ARMP protein. Applicant is requested to advise the examiner of all co-pending applications claiming subject matter related to E5-1 proteins.

Claim 73 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen, whose telephone number is (703) 308-0666. The examiner can normally be reached on Monday-Friday from 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, Ph.D., can be reached on (703) 308-4310. Official FAX communications may be directed to either (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER
GROUP 1800